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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,952	10/04/2004	Reddy Bandi Parthasaradhi	H1089/20015	3097

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
11/24/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,952	PARTHASARADHI ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicants dated Aug. 24, 2009 have been entered and considered carefully.

Claims 1-5 and newly added 5-7 are pending.

2. The rejection of claims 1-4 which are now applicable to claims 5-7 under 35 USC 112 first paragraph is maintained for reason of record.

Applicants argued that the specification provided methanol/chloroform and ethanol/chloroform for vacuum drying or spray drying to obtain the amorphous form of donepezil hydrochloride and giving such teaching, the quantity of experimentation required is not excessive in view of the subject matter of the claims.

Please note that the currently amended scope of solvents are:

> *"the alcohol is selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol and n-butyl alcohol and the chlorinated solvent is selected from the group consisting of chloroform, methylene dichloride, carbon tetrachloride and ethylene dichloride"*

In any combination or any ratio without limitation.

It was noted that two examples using methanol/chloroform in 50/50 v/v ratio and ethanol/chloroform in 60/50 v/v ratio. Such limited exemplification does not warrant the claimed scope since it was provided in the record the O'Hara reference, that one having ordinary skill in the art would recognized that "optimization" of solvent evaporation is an "unpredictable" parameter. Attorney provided no factual support that the narrow variation (methanol and ethanol) and narrow ratio can predict such claimed scope of unlimited choices of mixing and ratio of all the solvents.

3. The rejection of claims 1 and 4 under 35 USC 102(e) Over Vidyadhar '765 is maintained for reason of record.

The gist of applicants argument is that the examiner did not provide any evidence that the *in situ* mixed solvents of methylene chloride and methanol would be the same as the "pre-mixed" solvents of the claims.

Please note that, it is well recognized in the chemical art that methanol and methylene dichloride are material that will be fully miscible with organic solvents (see Merck Index #5814 methanol "miscible with most organic solvents", #5932 methylene chloride "miscible with alcohol"). Such miscible solvents whether mixed in situ or pre-mixed would not be different since they are miscible with each other. Applicants provided no factual evidence that why the pre-mixed methanol/methylene chloride and the in situ mixed methanol/methylene chloride would be different as to be not inherently mixture of the two material.

4. The rejection of claims 1-4 under 35 USC 103(a) over Vidyadhar '765 in view of Imai '864 or over sugimoto '841 or vidyadhar '765 or imain '864 in view of Lieberman and Brittain are applicable to the newly added claims 5-7 and maintained for reason of record.

It was clearly delineated in the record that:

Determination of the scope and content of the prior art (MPEP §2141.01)

Sugimoto et al. (col. 34 example 4) or Vijyadhar et al.'765 (col. 4, example 2) disclosed process of making donepezil hydrochloride of the claims. Imai et al. '864 disclosed multiple variations of modifying the process of making donepezil hydrochloride to obtain variations of crystalline and pure forms of the compound.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art processes and the instant claimed process is that the products being made are crystalline or solids; using mixtures of more limited solvent combinations; and/or the method of solvent removal being particularly vacuum drying or spray drying. It is conventionally known that donepezil hydrochloride is soluble in a variety of solvents (see Imai et al. '864 entire document). It is a conventional teaching that amorphous is more desirable than crystalline form when formulation into pharmaceutical compositions (see Lieberman p.463 last paragraph) and the conventional process for obtaining amorphous material are spray drying or vacuum drying i.e. lyophilization.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of Sugimoto '841 or Vijyadhar '765 and the above references by Imai et al. '864, Lieberman and Brittain would be in possession of the instant claims because a proven process of making donepezil hydrochloride in a purified form was disclosed by Sugimoto '841, Vijyadhar '765 or Imai '864. One having ordinary skill in the art in possession of the purified crystalline or solid material of the compound donepezil

hydrochloride would be motivated to prepare an amorphous form of the product because it is conventional state of the art that *"Theoretical considerations predict that amorphous solids* ***will*** *in general, be better absorbed than will crystalline ones"* (see Liberman p.463) and the procedure for obtaining amorphous forms have been conventionally well delineated using a spray drying or vacuum drying process (Brittain).

In view of factual evidence provided supra, one having ordinary skill, being motivated by obtaining a better absorbed amorphous form, would pick and choose any of the conventional combinations of solvents wherein donepezil hydrochloride is soluble, then, employ any one of the solvent removing technique for solvent reduction depending on resource and availability, with the expectation of obtaining an "amorphous" form of the product; the claims would have been obvious because an ordinary skilled person "has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." KSR 82 USPQ2d 1385, 1390.

The gist of applicants argument is that there is no suggestion of the prior art to use a mixture of solvents. Applicants are self conflicting because on one hand applicants argued that given an example of using methanol and chloroform, the employing of other solvents is a "quantity of experimentation required is not excessive in view of the subject matter" which supports the prima facie obviousness between the prior art and the instant claims since the sole different is using various solvents of using mixture of various solvents without limitation. On the other hand, applicants argued that, using different solvents is not obvious because changing solvents would not be motivated. It must be consistent with respect to applicants' argument, if the use of the exemplified solvent mixture provided any unexpected result which would not be due to the ordinary picking and choosing of the various common laboratory solvents such as methanol and chloroform, such unexpected results was not provided in the record. And if such mixture is unexpected, then, the broad scope of unlimited picking and choosing solvents with unlimited ratio cannot be enabling. Mere argument unsupported by factual evidence is entitled to little weight. In re Lindner 173 USPQ 356.

4. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Nov. 9, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625